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(71) Applicant *(for all designated States except US)*: **ANTHROGENESIS CORPORATION** [US/US]; 45 Horsehill Rd., Cedar Knolls, NJ 07927 (US).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **EDINGER, James, W.** [US/US]; 273 Leonardville Road, Belford, NJ 07718 (US). **HARIRI, Robert, J.** [US/US]; 5 Heritage Road, Florham Park, NJ 07932 (US). **WANG, Jia-Lun** [SE/US]; 212 Rabbit Run Road, Cherry Hill, NJ 08003 (US). **YE, Qian** [US/US]; 10 Mount Haven Drive, Livingston, NJ 07039 (US). **LABAZZO, Kristen, S.** [US/US]; 50 Newbrook Lane, Springfield, NJ 07081 (US). **PEREIRA, Marian** [US/US]; 8 Mohawk Drive, Cranford, NJ 07016 (US). **ABRAMSON, Sascha, Dawn** [US/US]; 609A Marlborough Common, Hillsborough, NJ 08844 (US).

(74) Agents: **INSOGNA, Anthony, M** et al.; Jones Day, 222 East 41st Street, New York, NY 10017-6702 (US).

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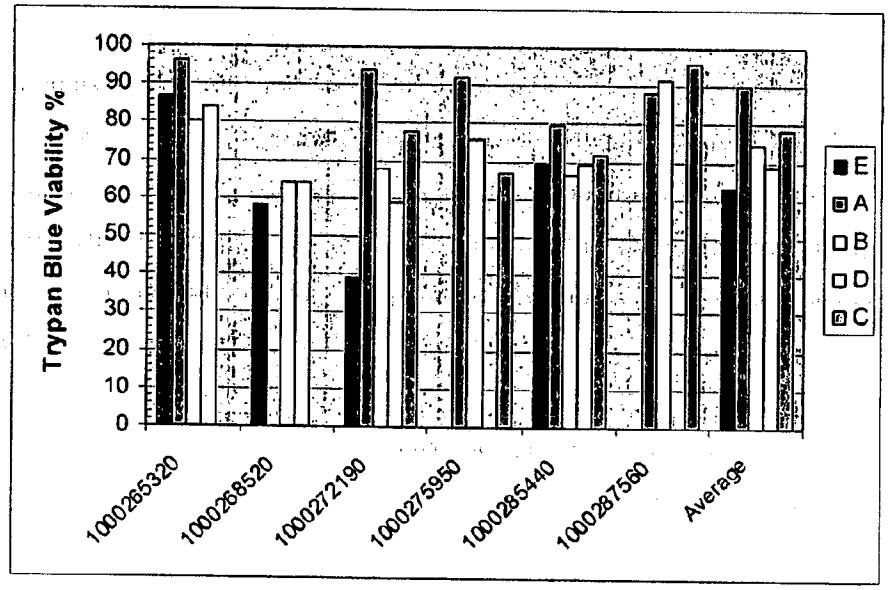
(54) Title: METHODS AND COMPOSITIONS FOR TREATMENT OF BONE DEFECTS WITH PLACENTAL CELL POPULATIONS



(57) Abstract: Provided herein are methods of using adherent placental stem cells and placental stem cell populations, and methods of culturing, proliferating and expanding the same. Also provided herein are methods of differentiating the placental stem cells. Further provided herein are methods of using the placental stem cells to formulate implantable or injectable compositions suitable for administration to a subject. Still further provided herein are provides methods for treating bone defects with stem cells and compositions comprising stem cells.

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METHODS AND COMPOSITIONS FOR TREATMENT OF BONE DEFECTS WITH PLACENTAL CELL POPULATIONS

1. FIELD

[0001] Provided herein are isolated placental cells, *e.g.*, placental perfusate, adherent and nonadherent placental stem cells, populations of placental stem cells, compositions comprising the stem cells, methods of obtaining the stem cells, methods of formulating compositions comprising the stem cells, and methods of treating bone defects with the stem cells and compositions.

2. BACKGROUND

[0002] Human stem cells are totipotential or pluripotential precursor cells capable of generating a variety of mature human cell lineages. Evidence exists that demonstrates that stem cells can be employed to repopulate many, if not all, tissues and restore physiologic and anatomic functionality.

[0003] Many different types of mammalian stem cells have been characterized. *See, e.g.*, Caplan *et al.*, U.S. Patent No. 5,486,359 (human mesenchymal stem cells); Boyse *et al.*, U.S. Patent No. 5,004,681 (fetal and neonatal hematopoietic stem and progenitor cells); Boyse *et al.*, U.S. 5,192,553 (same); Beltrami *et al.*, *Cell* 114(6):763-766 (2003) (cardiac stem cells); Forbes *et al.*, *J. Pathol.* 197(4):510-518 (2002) (hepatic stem cells). Umbilical cord blood, and total nucleated cells derived from cord blood, have been used in transplants to restore, partially or fully, hematopoietic function in patients who have undergone ablative therapy.

3. SUMMARY

[0004] Provided herein are isolated placental cells, *e.g.*, placental perfusate, adherent or nonadherent placental stem cells, populations of placental stem cells, compositions comprising the cells, methods of obtaining the placental cells, methods of formulating the compositions, and methods of using the cells to treat bone defects.

[0005] Provided herein are isolated stem cells, and cell populations comprising such stem cells, wherein the stem cells are present in, and isolatable from placental tissue (*e.g.*, amnion, chorion, placental cotyledons, umbilical cord, *etc.*), that are useful in the repair of bone

defects. The placental stem cells exhibit one or more characteristics of a stem cell (*e.g.*, exhibit markers associated with stem cells, replicate at least 10-20 times in culture in an undifferentiated state, differentiate into adult cells representative of the three germ layers, *etc.*), and can adhere to a tissue culture substrate (*e.g.*, tissue culture plastic such as the surface of a tissue culture dish or multiwell plate).

[0006] In one embodiment, provided herein is an isolated placental stem cell that is nonadherent. In certain embodiments, the isolated stem cell is $CD34^+$. In certain embodiments, the isolated stem cell is $CD44^-$. In certain embodiments, the isolated stem cell is $CD34^+$ and $CD44^-$. In certain embodiments, the isolated stem cell is $CD9^+$, $CD54^+$, $CD90^+$, or $CD166^+$. In certain embodiments, the isolated stem cell is $CD9^+$, $CD54^+$, $CD90^+$, and $CD166^+$. In certain embodiments, the isolated stem cell is $CD31^+$, $CD117^+$, $CD133^+$, or $CD200^+$. In certain embodiments, the isolated stem cell is $CD31^+$, $CD117^+$, $CD133^+$, and $CD200^+$. In certain embodiments, the isolated stem cell has been isolated from a human placenta by enzymatic digestion. In certain embodiments, the isolated stem cell has been isolated from a human placenta by perfusion. In certain embodiments, the isolated stem cell facilitates formation of a mineralized matrix in a population of placental cells when said population is cultured under conditions that allow the formation of a mineralized matrix.

[0007] In another embodiment, provided herein is a population of isolated placental cells that are nonadherent. In certain embodiments, the population comprises stem cells that are $CD34^+$. In certain embodiments, the population comprises stem cells that are $CD44^-$. In certain embodiments, the population comprises stem cells that are $CD34^+$ and $CD44^-$. In certain embodiments, the population comprises stem cells that are $CD9^+$, $CD54^+$, $CD90^+$, or $CD166^+$. In certain embodiments, the population comprises stem cells that are $CD9^+$, $CD54^+$, $CD90^+$, and $CD166^+$. In certain embodiments, the population comprises stem cells that are $CD31^+$, $CD117^+$, $CD133^+$, or $CD200^+$. In certain embodiments, the population comprises stem cells that are $CD31^+$, $CD117^+$, $CD133^+$, and $CD200^+$. In certain embodiments, the population comprises stem cells, wherein at least about 70% of said cells are $CD34^+$ and $CD44^-$ stem cells. In certain embodiments, the population comprises stem cells, wherein at least about 90% of said cells are $CD34^+$ and $CD44^-$ stem cells. In certain embodiments, the population has been expanded. In certain embodiments, the population has been passaged at least once. In certain embodiments, the population has been passaged at least five times. In certain embodiments, the population has been passaged at least ten times. In certain embodiments, the population has been passaged at least twenty times. In certain embodiments, the population forms, or facilitates the formation of, a mineralized matrix in a

population of placental cells when said population is cultured under conditions that allow the formation of a mineralized matrix.

[0008] In another aspect, provided herein is a population of isolated placental stem cells that are $CD34^+$ and $CD44^-$. In certain embodiments, the stem cells are $CD9^+$, $CD54^+$, $CD90^+$, or $CD166^+$. In certain embodiments, the stem cells are $CD9^+$, $CD54^+$, $CD90^+$, and $CD166^+$. In certain embodiments, the stem cells are $CD31^+$, $CD117^+$, $CD133^+$, or $CD200^+$. In certain embodiments, the stem cells are $CD31^+$, $CD117^+$, $CD133^+$, and $CD200^+$. In certain embodiments, at least about 70% of the stem cells are $CD34^+$ and $CD44^-$ stem cells. In certain embodiments, at least about 90% of the stem cells are $CD34^+$ and $CD44^-$ stem cells. In certain embodiments, the population has been expanded. In certain embodiments, the population has been passaged at least once. In certain embodiments, the population has been passaged at least five times. In certain embodiments, the population has been passaged at least ten times. In certain embodiments, the population has been passaged at least twenty times. In certain embodiments, the population forms, or facilitates the formation of, a mineralized matrix in a population of placental cells when said population is cultured under conditions that allow the formation of a mineralized matrix.

[0009] In one embodiment, provided herein is an isolated placental stem cell that is $CD200^+$ or $HLA\text{-}G^+$. In a specific embodiment, the stem cell is adherent. In another specific embodiment, said cell is $CD200^+$ and $HLA\text{-}G^+$. In a specific embodiment, said stem cell is $CD73^+$ and $CD105^+$. In another specific embodiment, said stem cell is $CD34^-$, $CD38^-$ or $CD45^-$. In another specific embodiment, said stem cell is $CD34^-$, $CD38^-$ and $CD45^-$. In another specific embodiment, said stem cell is $CD34^-$, $CD38^-$, $CD45^-$, $CD73^+$ and $CD105^+$. In another specific embodiment, said stem cell facilitates the formation of one or more embryoid-like bodies from a population of isolated placental cells comprising placental stem cells when said population is cultured under conditions that allow formation of embryoid-like bodies.

[0010] In another embodiment, provided herein is a population of isolated placental cells comprising $CD200^+$, $HLA\text{-}G^+$ stem cells. In a specific embodiment, said stem cells are adherent. In various embodiments, at least about 10%, at least about 20%, at least about 30%, at least about 40%, at least about 50% at least about 60%, at least about 70%, at least about 80%, at least about 90%, or at least about 95% or more of said isolated placental cells are $CD200^+$, $HLA\text{-}G^+$ stem cells. In a specific embodiment of the above populations, said stem cells are $CD73^+$ and $CD105^+$. In another specific embodiment, said stem cells are $CD34^-$, $CD38^-$ or $CD45^-$. In a more specific embodiment, said stem cells are $CD34^-$, $CD38^-$,

$CD45^-$, $CD73^+$ and $CD105^+$. In other specific embodiments, said population has been expanded, *e.g.*, passaged at least once, at least three times, at least five times, at least 10 times, at least 15 times, or at least 20 times. In another specific embodiment, said population forms one or more embryoid-like bodies when cultured under conditions that allow formation of embryoid-like bodies.

[0011] In another embodiment, provided herein is an isolated placental stem cell that is $CD73^+$, $CD105^+$, and $CD200^+$. In a specific embodiment, said stem cell is adherent. In another specific embodiment, said stem cell is HLA-G^+. In another specific embodiment, said stem cell is $CD34^-$, $CD38^-$ or $CD45^-$. In another specific embodiment, said stem cell is $CD34^-$, $CD38^-$ and $CD45^-$. In a more specific embodiment, said stem cell is $CD34^-$, $CD38^-$, $CD45^-$, and HLA-G^+. In another specific embodiment, said stem cell facilitates development of one or more embryoid-like bodies from a population of isolated placental cells comprising the stem cell when said population is cultured under conditions that allow formation of embryoid-like bodies.

[0012] In another embodiment, provided herein is a population of isolated placental cells comprising $CD73^+$, $CD105^+$, $CD200^+$ stem cells. In a specific embodiment, said stem cells are adherent. In various embodiments, at least about 10%, at least about 20%, at least about 30%, at least about 40%, at least about 50% at least about 60%, at least about 70%, at least about 80%, at least about 90%, or at least about 95% of said isolated placental cells are $CD73^+$, $CD105^+$, $CD200^+$ stem cells. In a specific embodiment of said populations, said stem cells are HLA-G^+. In another specific embodiment, said stem cells are $CD34^-$, $CD38^-$ or $CD45^-$. In another specific embodiment, said stem cells are $CD34^-$, $CD38^-$ and $CD45^-$. In a more specific embodiment, said stem cells are $CD34^-$, $CD38^-$, $CD45^-$, and HLA-G^+. In other specific embodiments, said population has been expanded, for example, passaged at least once, at least three times, at least five times, at least 10 times, at least 15 times, or at least 20 times. In another specific embodiment, said population forms one or more embryoid-like bodies in culture under conditions that allow formation of embryoid-like bodies.

[0013] Also provided herein is an isolated placental stem cell that is $CD200^+$ and OCT-4^+. In a specific embodiment, said stem cell is adherent. In another specific embodiment, the stem cell is $CD73^+$ and $CD105^+$. In another specific embodiment, said stem cell is HLA-G^+. In another specific embodiment, said stem cell is $CD34^-$, $CD38^-$ or $CD45^-$. In another specific embodiment, said stem cell is $CD34^-$, $CD38^-$ and $CD45^-$. In a more specific embodiment, said stem cell is $CD34^-$, $CD38^-$, $CD45^-$, $CD73^+$, $CD105^+$ and HLA-G^+. In another specific embodiment, said stem cell facilitates the formation of one or more embryoid-like bodies

from a population of isolated placental cells comprising placental stem cells when said population is cultured under conditions that allow formation of embryoid-like bodies.

[0014] In another embodiment, provided herein is a population of isolated placental cells comprising $CD200^+$, $OCT\text{-}4^+$ placental stem cells. In a specific embodiment, the stem cells are adherent. In various embodiments, at least about 10%, at least about 20%, at least about 30%, at least about 40%, at least about 50% at least about 60%, at least about 70%, at least about 80%, at least about 90%, or at least about 95% of said isolated placental cells are $CD200^+$, $OCT\text{-}4^+$ stem cells. In a specific embodiment of the above populations, said stem cells are $CD73^+$ and $CD105^+$. In another specific embodiment, said stem cells are $HLA\text{-}G^+$. In another specific embodiment, said stem cells are $CD34^-$, $CD38^-$ and $CD45^-$. In a more specific embodiment, said stem cells are $CD34^-$, $CD38^-$, $CD45^-$, $CD73^+$, $CD105^+$ and $HLA\text{-}G^+$. In other specific embodiments, said population has been expanded, for example, has been passaged at least once, at least three times, at least five times, at least 10 times, at least 15 times, or at least 20 times. In another specific embodiment, said population forms one or more embryoid-like bodies when cultured under conditions that allow the formation of embryoid-like bodies.

[0015] In another embodiment, provided herein is an isolated placental stem cell that is $CD73^+$ and $CD105^+$ and which facilitates the formation of one or more embryoid-like bodies in a population of isolated placental cells comprising said stem cell when said population is cultured under conditions that allow formation of embryoid-like bodies. In a specific embodiment, said stem cell is adherent. In another specific embodiment, said stem cell is $CD34^-$, $CD38^-$ or $CD45^-$. In another specific embodiment, said stem cell is $CD34^-$, $CD38^-$ and $CD45^-$. In another specific embodiment, said stem cell is $OCT4^+$. In a more specific embodiment, said stem cell is OCT4+, $CD34^-$, $CD38^-$ and $CD45^-$.

[0016] Further provided herein is a population of isolated placental cells comprising $CD73^+$, $CD105^+$ placental stem cells, wherein said population forms one or more embryoid-like bodies under conditions that allow formation of embryoid-like bodies. In a specific embodiment, said stem cells are adherent. In various embodiments, at least about 10%, at least about 20%, at least about 30%, at least about 40%, at least about 50% at least about 60%, at least about 70%, at least about 80%, at least about 90%, or at least about 95% of said isolated placental cells are $CD73^+$, $CD105^+$ stem cells. In a specific embodiment of the above populations, said stem cells are $CD34^-$, $CD38^-$ or $CD45^-$. In another specific embodiment, said stem cells are $CD34^-$, $CD38^-$ and $CD45^-$. In another specific embodiment, said stem cells are $OCT\text{-}4^+$. In a more specific embodiment, said stem cells are $OCT\text{-}4^+$, $CD34^-$,

$CD38^-$ and $CD45^-$. In other specific embodiments, said population has been expanded, for example, has been passaged at least once, at least three times, at least five times, at least 10 times, at least 15 times, or at least 20 times.

[0017] Further provided herein is an isolated placental stem cell that is $CD73^+$, $CD105^+$ and $HLA\text{-}G^+$. In a specific embodiment, said stem cell is adherent. In another specific embodiment, said stem cell is $CD34^-$, $CD38^-$ or $CD45^-$. In another specific embodiment, said stem cell is $CD34^-$, $CD38^-$ and $CD45^-$. In another specific embodiment, said stem cell is $OCT\text{-}4^+$. In another specific embodiment, said stem cell is $CD200^+$. In a more specific embodiment, said stem cell is $CD34^-$, $CD38^-$, $CD45^-$, $OCT\text{-}4^+$ and $CD200^+$. In another specific embodiment, said stem cell facilitates the formation of one or more embryoid-like bodies from a population of isolated placental cells comprising placental stem cells in culture under conditions that allow formation of embryoid-like bodies.

[0018] Further provided herein is a population of isolated placental cells comprising $CD73^+$, $CD105^+$ and $HLA\text{-}G^+$ placental stem cells. In a specific embodiment, the stem cells are adherent. In various embodiments, at least about 10%, at least about 20%, at least about 30%, at least about 40%, at least about 50% at least about 60%, at least about 70%, at least about 80%, at least about 90%, or at least about 95% of said isolated placental cells are $CD73^+$, $CD105^+$ and $HLA\text{-}G^+$ stem cells. In a specific embodiment of the above populations, said stem cells are $CD34^-$, $CD38^-$ or $CD45^-$. In another specific embodiment, said stem cells are $CD34^-$, $CD38^-$ and $CD45^-$. In another specific embodiment, said stem cells are $OCT\text{-}4^+$. In another specific embodiment, said stem cells are $CD200^+$. In a more specific embodiment, said stem cells are $CD34^-$, $CD38^-$, $CD45^-$, $OCT\text{-}4^+$ and $CD200^+$. In another specific embodiment, said population has been expanded, for example, has been passaged at least once, at least three times, at least five times, at least 10 times, at least 15 times, or at least 20 times. In another specific embodiment, said population forms embryoid-like bodies when cultured under conditions that allow the formation of embryoid-like bodies.

[0019] Further provided herein is an isolated placental stem cell that is $OCT\text{-}4^+$ and which facilitates formation of one or more embryoid-like bodies in a population of isolated placental cells comprising said stem cell when cultured under conditions that allow formation of embryoid-like bodies. In a specific embodiment, said stem cell is adherent. In another specific embodiment, said stem cell is $CD73^+$ and $CD105^+$. In another specific embodiment, said stem cell is $CD34^-$, $CD38^-$, or $CD45^-$. In another specific embodiment, said stem cell is $CD200^+$. In a more specific embodiment, said stem cell is $CD73^+$, $CD105^+$, $CD200^+$, $CD34^-$, $CD38^-$, and $CD45^-$.

[0020] Also provided herein is a population of isolated placental cells comprising OCT-4$^+$ placental stem cells, wherein said population forms one or more embryoid-like bodies when cultured under conditions that allow the formation of embryoid-like bodies. In a specific embodiment, the stem cells are adherent. In various embodiments, at least about 10%, at least about 20%, at least about 30%, at least about 40%, at least about 50% at least about 60%, at least about 70%, at least about 80%, at least about 90%, or at least about 95% of said isolated placental cells are OCT4$^+$ stem cells. In a specific embodiment of the above populations, said stem cells are CD73$^+$ and CD105$^+$. In another specific embodiment, said stem cells are CD34$^-$, CD38$^-$, or CD45$^-$. In another specific embodiment, said stem cells are CD200$^+$. In a more specific embodiment, said stem cells are CD73$^+$, CD105$^+$, CD200$^+$, CD34$^-$, CD38$^-$, and CD45$^-$. In another specific embodiment, said population has been expanded, for example, passaged at least once, at least three times, at least five times, at least 10 times, at least 15 times, or at least 20 times.

[0021] Further provided herein is an isolated population of the adherent or nonadherent placental stem cells described herein that is produced according to a method comprising perfusing a mammalian placenta that has been drained of cord blood and perfused to remove residual blood; perfusing said placenta with a perfusion solution; and collecting said perfusion solution, wherein said perfusion solution after perfusion comprises a population of placental cells that comprises placental stem cells; and isolating a plurality of said placental stem cells from said population of cells. In a specific embodiment, the perfusion solution is passed through both the umbilical vein and umbilical arteries and collected after it exudes from the placenta. In another specific embodiment, the perfusion solution is passed through the umbilical vein and collected from the umbilical arteries, or passed through the umbilical arteries and collected from the umbilical vein.

[0022] Further provided herein is an isolated placental stem cell, or isolated population of the placental stem cells, described herein that is produced according to a method comprising digesting placental tissue with a tissue-disrupting enzyme to obtain a population of placental cells comprising placental stem cells, and isolating a plurality of placental stem cells from the remainder of said placental cells. In specific embodiments, said placental tissue is a whole placenta, an amniotic membrane, chorion, a combination of amnion and chorion, or a combination of any of the foregoing. In other specific embodiment, the tissue-disrupting enzyme is trypsin or collagenase.

[0023] In more specific embodiments, provided herein is an isolated placental stem cell, wherein said stem cell expresses one or more genes at a detectably higher level than a bone

marrow-derived mesenchymal stem cell, wherein said one or more genes are ACTG2, ADARB1, AMIGO2, ATRS-1, B4GALT6, BCHE, C11orf9, CD200, COL4A1, COL4A2, CPA4, DMD, DSC3, DSG2, ELOVL2, F2RL1, FLJ10781, GATA6, GPR126, GPRC5B, ICAM1, IER3, IGFBP7, IL1A, IL6, IL18, KRT18, KRT8, LIPG, LRAP, MATN2, MEST, NFE2L3, NUAK1, PCDH7, PDLIM3, PJP2, RTN1, SERPINB9, ST3GAL6, ST6GALNAC5, SLC12A8, TCF21, TGFB2, VTN, and/or ZC3H12A, and wherein said bone marrow derived stem cell has undergone a number of passages in culture equivalent to a number of passages for said placental stem cell. In a more specific embodiment, said placental stem cell expresses ACTG2, ADARB1, AMIGO2, ATRS-1, B4GALT6, BCHE, C11orf9, CD200, COL4A1, COL4A2, CPA4, DMD, DSC3, DSG2, ELOVL2, F2RL1, FLJ10781, GATA6, GPR126, GPRC5B, ICAM1, IER3, IGFBP7, IL1A, IL6, IL18, KRT18, KRT8, LIPG, LRAP, MATN2, MEST, NFE2L3, NUAK1, PCDH7, PDLIM3, PJP2, RTN1, SERPINB9, ST3GAL6, ST6GALNAC5, SLC12A8, TCF21, TGFB2, VTN, and ZC3H12A at a detectably higher level than a bone marrow-derived mesenchymal stem cell.

[0024] In more specific embodiments, also provided herein is a population of isolated placental stem cells, wherein said population of stem cells express one or more genes at a detectably higher level than a population of bone marrow-derived mesenchymal stem cells, wherein said one or more genes are ACTG2, ADARB1, AMIGO2, ATRS-1, B4GALT6, BCHE, C11orf9, CD200, COL4A1, COL4A2, CPA4, DMD, DSC3, DSG2, ELOVL2, F2RL1, FLJ10781, GATA6, GPR126, GPRC5B, ICAM1, IER3, IGFBP7, IL1A, IL6, IL18, KRT18, KRT8, LIPG, LRAP, MATN2, MEST, NFE2L3, NUAK1, PCDH7, PDLIM3, PJP2, RTN1, SERPINB9, ST3GAL6, ST6GALNAC5, SLC12A8, TCF21, TGFB2, VTN, and/or ZC3H12A, and wherein said population of bone marrow derived stem cells has undergone a number of passages in culture equivalent to a number of passages for said placental stem cell, and wherein said population of bone marrow-derived mesenchymal stem cells has a number of cells equivalent to said population of isolated stem cells. In a more specific embodiment, the population of isolated stem cells expresses ACTG2, ADARB1, AMIGO2, ATRS-1, B4GALT6, BCHE, C11orf9, CD200, COL4A1, COL4A2, CPA4, DMD, DSC3, DSG2, ELOVL2, F2RL1, FLJ10781, GATA6, GPR126, GPRC5B, ICAM1, IER3, IGFBP7, IL1A, IL6, IL18, KRT18, KRT8, LIPG, LRAP, MATN2, MEST, NFE2L3, NUAK1, PCDH7, PDLIM3, PJP2, RTN1, SERPINB9, ST3GAL6, ST6GALNAC5, SLC12A8, TCF21, TGFB2, VTN, and ZC3H12A at a detectably higher level than said population of isolated bone marrow-derived mesenchymal stem cells.

[0025] Also provided herein are compositions that comprise one or more of the placental cells, *e.g.*, placental perfusate, placental perfusate cells or placental stem cells, provided herein, wherein the cells have been isolated from the placenta. In preferred embodiments, the compositions comprising placental cells are useful for the repair of bone defects. Thus, provided herein is a composition comprising placental perfusate, or cells isolated from placental perfusate, *e.g.*, total nucleated cells from placental perfusate.

[0026] In one aspect, provided herein is a composition comprising placental perfusate or placental perfusate cells, *e.g.*, total nucleated cells from placental perfusate.

[0027] Further provided herein is a composition comprising a placental stem cell, wherein said stem cell is an isolated placental stem cell that is nonadherent. In certain embodiments, the stem cell is $CD34^+$. In certain embodiments, the stem cell is $CD44^-$. In certain embodiments, the stem cell is $CD34^+$ and $CD44^-$. In certain embodiments, the stem cell is $CD9^+$, $CD54^+$, $CD90^+$, or $CD166^+$. In certain embodiments, the stem cell is $CD9^+$, $CD54^+$, $CD90^+$, and $CD166^+$. In certain embodiments, the stem cell is $CD31^+$, $CD117^+$, $CD133^+$, or $CD200^+$. In certain embodiments, the stem cell is $CD31^+$, $CD117^+$, $CD133^+$, and $CD200^+$. In certain embodiments, the stem cell has been isolated from a human placenta by enzymatic digestion. In certain embodiments, the stem cell has been isolated from a human placenta by perfusion. In certain embodiments, the cell facilitates formation of a mineralized matrix in a population of placental cells when said population is cultured under conditions that allow the formation of a mineralized matrix.

[0028] In another aspect, provided herein is a composition comprising a placental stem cell, wherein said stem cell is an isolated stem cell that is $CD34^+$ and $CD44^-$. In certain embodiments, the stem cell is $CD9^+$, $CD54^+$, $CD90^+$, or $CD166^+$. In certain embodiments, the stem cell is $CD9^+$, $CD54^+$, $CD90^+$, and $CD166^+$. In certain embodiments, the stem cell is $CD31^+$, $CD117^+$, $CD133^+$, or $CD200^+$. In certain embodiments, the stem cell is $CD31^+$, $CD117^+$, $CD133^+$, and $CD200^+$. In certain embodiments, the stem cell has been isolated from a human placenta by enzymatic digestion. In certain embodiments, the stem cell has been isolated from a human placenta by perfusion. In certain embodiments, the cell facilitates formation of a mineralized matrix in a population of placental cells when said population is cultured under conditions that allow the formation of a mineralized matrix.

[0029] In certain embodiments, the composition comprises an isolated stem cell provided herein and a compound that induces the differentiation of said stem cell into an osteogenic cell. In certain embodiments, the composition comprises an isolated stem cell, or a population of isolated stem cells, provided herein, and a compound that induces the

differentiation of a plurality of stem cells in said population of stem cells into osteogenic cells. In certain embodiments, the compound is dexamethasone or ascorbic acid.

[0030] In certain embodiments, provided herein is a composition comprising an isolated placental stem cell, wherein said stem cell is $CD200^+$ and $HLA\text{-}G^+$. In a specific embodiment, the stem cell is adherent. In another specific embodiment, said stem cell is $CD73^+$ and $CD105^+$. In another specific embodiment, said stem cell is $CD34^-$, $CD38^-$ or $CD45^-$. In another specific embodiment, said stem cell is $CD34^-$, $CD38^-$ and $CD45^-$. In a more specific embodiment, said stem cell is $CD34^-$, $CD38^-$, $CD45^-$, $CD73^+$, $CD105^+$, $CD200^+$ and $HLA\text{-}G^+$.

[0031] In another embodiment, provided herein is a composition comprising an isolated placental stem cell, wherein said stem cell is $CD73^+$, $CD105^+$ and $CD200^+$. In a specific embodiment, the stem cell is adherent. In another specific embodiment, said stem cell is $HLA\text{-}G^+$. In another specific embodiment, said stem cell is $CD34^-$, $CD38^-$ or $CD45^-$. In another specific embodiment, said stem cell is $CD34^-$, $CD38^-$ and $CD45^-$. In another specific embodiment, said stem cell is $CD34^-$, $CD38^-$, $CD45^-$, and $HLA\text{-}G^+$.

[0032] In another embodiment, provided herein is a composition comprising an isolated placental stem cell, wherein said stem cell is $CD200^+$ and $OCT\text{-}4^+$. In a specific embodiment, the stem cell is adherent. In another specific embodiment, said stem cell is $CD73^+$ and $CD105^+$. In another specific embodiment, said stem cell is $HLA\text{-}G^+$. In another specific embodiment, said stem cell is $CD34^-$, $CD38^-$ or $CD45^-$. In another specific embodiment, said stem cell is $CD34^-$, $CD38^-$ and $CD45^-$. In another specific embodiment, said stem cell is $CD34^-$, $CD38^-$, $CD45^-$, $CD73^+$, $CD105^+$, and $HLA\text{-}G^+$.

[0033] In another embodiment, provided herein is a composition comprising an isolated placental stem cell that is $CD73^+$ and $CD105^+$, wherein said stem cell facilitates formation of an embryoid-like body in a population of isolated placental cells comprising said stem cell under conditions that allow the formation of an embryoid-like body. In a specific embodiment, the stem cell is adherent. In another specific embodiment, said stem cell is $CD34^-$, $CD38^-$ or $CD45^-$. In another specific embodiment, said stem cell is $OCT\text{-}4^+$. In another specific embodiment, said stem cell is $CD200^+$. In another specific embodiment, said stem cell is OCT-4+, $CD200^+$, $CD34^-$, $CD38^-$ and $CD45^-$.

[0034] In yet another embodiment, provided herein is a composition comprising an isolated placental stem cell that is $CD73^+$, $CD105^+$ and $HLA\text{-}G^+$. In a specific embodiment, the stem cell is adherent. In another specific embodiment, said stem cell is $CD34^-$, $CD38^-$ or $CD45^-$. In another specific embodiment, said stem cell is $OCT\text{-}4^+$. In another specific embodiment,

said stem cell is $CD200^+$. In another specific embodiment, said stem cell is OCT-4+, $CD200^+$, $CD34^-$, $CD38^-$ and $CD45^-$.

[0035] In another embodiment, provided herein is a composition comprising an isolated placental stem cell that is $OCT\text{-}4^+$, wherein said stem cell facilitates formation of an embryoid-like body in a population of isolated placental cells comprising said stem cell under conditions that allow the formation of an embryoid-like body. In a specific embodiment, said stem cell is $CD73^+$ and $CD105^+$. In another specific embodiment, said stem cell is $CD34^-$, $CD38^-$ and $CD45^-$. In another specific embodiment, said stem cell is $CD200^+$. In another specific embodiment, said stem cell is $CD73^+$, $CD105^+$, $CD200^+$, $CD34^-$, $CD38^-$ and $CD45^-$.

[0036] Further provided herein is a composition comprising a placental stem cells that expresses one or more genes at a detectably higher level than a bone marrow-derived mesenchymal stem cell, wherein said one or more genes are selected from the group consisting of ACTG2, ADARB1, AMIGO2, ATRS-1, B4GALT6, BCHE, C11orf9, CD200, COL4A1, COL4A2, CPA4, DMD, DSC3, DSG2, ELOVL2, F2RL1, FLJ10781, GATA6, GPR126, GPRC5B, ICAM1, IER3, IGFBP7, IL1A, IL6, IL18, KRT18, KRT8, LIPG, LRAP, MATN2, MEST, NFE2L3, NUAK1, PCDH7, PDLIM3, PJP2, RTN1, SERPINB9, ST3GAL6, ST6GALNAC5, SLC12A8, TCF21, TGFB2, VTN, and ZC3H12A, and wherein said bone marrow derived stem cell has undergone a number of passages in culture equivalent to a number of passages for said placental stem cell. In a more specific embodiment of the above composition, said stem cells express ACTG2, ADARB1, AMIGO2, ATRS-1, B4GALT6, BCHE, C11orf9, CD200, COL4A1, COL4A2, CPA4, DMD, DSC3, DSG2, ELOVL2, F2RL1, FLJ10781, GATA6, GPR126, GPRC5B, ICAM1, IER3, IGFBP7, IL1A, IL6, IL18, KRT18, KRT8, LIPG, LRAP, MATN2, MEST, NFE2L3, NUAK1, PCDH7, PDLIM3, PJP2, RTN1, SERPINB9, ST3GAL6, ST6GALNAC5, SLC12A8, TCF21, TGFB2, VTN, and ZC3H12A at a detectably higher level than a population of isolated bone marrow-derived mesenchymal stem cell, wherein said population of stem cells and said population of bone marrow-derived mesenchymal cells have equivalent numbers of cells.

[0037] In another specific embodiment, any of the foregoing compositions comprises a matrix. In a more specific embodiment, said matrix is a three-dimensional scaffold. In another more specific embodiment, said matrix comprises collagen, gelatin, laminin, fibronectin, pectin, ornithine, or vitronectin. In another more specific embodiment, the matrix is an amniotic membrane or an amniotic membrane-derived biomaterial. In another more specific embodiment, said matrix comprises an extracellular membrane protein. In another more specific embodiment, said matrix comprises a synthetic compound. In another

more specific embodiment, said matrix comprises a bioactive compound. In another more specific embodiment, said bioactive compound is a growth factor, cytokine, antibody, or organic molecule of less than 5,000 daltons. In certain embodiments, the matrix is a synthetic degradable polymer such as, for example, polylactic acid or polyglycolic acid. In certain embodiments, the matrix is an implantable scaffolding substrate. In certain embodiments, the implantable scaffolding substrate is selected from the group consisting of a β-tricalcium phosphate substrate, a β-tricalcium phosphate-collagen substrate, a collagen substrate, a calcium phosphate substrate, a mineralized human placental collagen substrate, a hyaluronic acid substrate, and a ceramic substrate. In certain embodiments, the implantable scaffolding substrate is a β-tricalcium phosphate substrate. In certain embodiments, the implantable scaffolding substrate is a β-tricalcium phosphate-collagen substrate. In certain embodiments, the implantable scaffolding substrate is a collagen substrate. In certain embodiments, the implantable scaffolding substrate is a calcium phosphate substrate. In certain embodiments, the implantable scaffolding substrate is a mineralized human placental collagen substrate.

[0038] In another embodiment, further provided herein is a composition comprising medium conditioned by any of the foregoing stem cells, or any of the foregoing stem cell populations. In a specific embodiment, any such composition comprises a stem cell that is not derived from a placenta. In a more specific embodiment, said stem cell is an embryonic stem cell. In another more specific embodiment, said stem cell is a mesenchymal stem cell. In another more specific embodiment, said stem cell is a bone marrow-derived stem cell. In another more specific embodiment, said stem cell is a hematopoietic progenitor cell. In another more specific embodiment, said stem cell is a somatic stem cell. In an even more specific embodiment, said somatic stem cell is a neural stem cell, a hepatic stem cell, a pancreatic stem cell, an endothelial stem cell, a cardiac stem cell, or a muscle stem cell.

[0039] In another aspect, provided herein is a composition comprising medium conditioned by a placental stem cell or population of placental stem cells provided herein. In certain embodiments, the composition comprises medium conditioned by a cell population, *e.g.*, a stem cell population, provided herein.

[0040] Also provided herein is a method of producing a cell population comprising selecting cells that do not adhere to a substrate, and isolating said cells from other cells to form a cell population. In certain embodiments, the method further comprises selecting cells that express CD34 and do not express CD44 and increasing the concentration of, *e.g.*, isolating said cells from other cells, to form a cell population.

[0041] In certain embodiments, provided herein is a method of producing a cell population, comprising selecting cells that (a) do not adhere to a substrate, (b) express CD34 and do not express CD44, and (c) facilitate the formation of mineralized matrix in a population of placental cells when said population is cultured under conditions that allow for the formation of a mineralized matrix; and isolating said cells from other cells to form a cell population. In certain embodiments, the substrate comprises fibronectin.

[0042] In certain embodiments, the method further comprises selecting cells that express CD9, CD29, CD54, CD90, CD166, or a combination of the foregoing.

[0043] In certain embodiments, the method further comprises selecting cells that express CD31, CD34, CD117, CD133, CD200, or a combination of the foregoing.

[0044] In certain embodiments, the selecting is accomplished using an antibody. In certain embodiments, the selecting is accomplished using flow cytometry. In certain embodiments, the selecting is accomplished using magnetic beads. In certain embodiments, the selecting is accomplished by fluorescence-activated cell sorting. In certain embodiments, the cell population is expanded.

[0045] In another aspect, provided herein is a population of nonadherent placental stem cells, wherein said cells have been cryopreserved, and wherein said population is contained within a container. In certain embodiments, the stem cells are $CD34^+$ and $CD44^-$. In certain embodiments, the cells have been cryopreserved, and wherein said population is contained within a container, and wherein said stem cells form a mineralized matrix when cultured under conditions allowing the formation of a mineralized matrix. In certain embodiments, the container is a bag suitable for the intravenous delivery of a liquid. In certain embodiments, the population comprises 1×10^6 said stem cells. In certain embodiments, the population comprises 5×10^6 said stem cells. In certain embodiments, the population comprises 1×10^7 said stem cells. In certain embodiments, the population comprises 5×10^7 said stem cells. In certain embodiments, the population comprises 1×10^8 said stem cells. In certain embodiments, the population comprises 5×10^8 said stem cells. In certain embodiments, the population comprises 1×10^9 said stem cells. In certain embodiments, the population comprises 5×10^9 said stem cells. In certain embodiments, the population comprises 1×10^{10} said stem cells. In certain embodiments, the stem cells have been passaged no more than 5 times. In certain embodiments, the stem cells have been passaged no more than 10 times. In certain embodiments, the stem cells have been passaged no more than 15 times. In certain embodiments, the stem cells have been passaged no more than 20

times. In certain embodiments, the stem cells have been expanded within said container. In certain embodiments, the population is contained in a 0.9% NaCl solution.

[0046] In another aspect, provided herein is a method of producing osteogenic cells with the ability to mineralize matrix, comprising culturing a plurality of stem cells provided herein or a population of isolated stem cells provided herein, under conditions in which said stem cells differentiate into osteogenic cells, said culturing being for a time sufficient for said osteogenic cells to produce, or facilitate the production of, detectable amounts of mineralized matrix rich in calcium and/or phosphate. In certain embodiments, the osteogenic cells produce bone.

[0047] In still another aspect, provided herein is a method for formulating a matrix, comprising combining a population of stem cells provided herein with an implantable scaffolding substrate. In certain embodiments, the stem cells are nonadherent. In certain embodiments, the stem cells are $CD34^+$. In certain embodiments, the stem cells are $CD44^-$. In certain embodiments, the stem cells are $CD34^+$ and $CD44^-$. In certain embodiments, the stem cells are $CD9^+$, $CD54^+$, $CD90^+$, or $CD166^+$. In certain embodiments, the stem cells are $CD9^+$, $CD54^+$, $CD90^+$, and $CD166^+$. In certain embodiments, the stem cells are $CD31^+$, $CD117^+$, $CD133^+$, or $CD200^+$. In certain embodiments, the stem cells are $CD31^+$, $CD117^+$, $CD133^+$, and $CD200^+$. In certain embodiments, at least about 70% of the stem cells are $CD34^+$ and $CD44^-$ stem cells. In certain embodiments, at least about 90% of the stem cells are $CD34^+$ and $CD44^-$ stem cells. In certain embodiments, the population comprises 1×10^6 said stem cells. In certain embodiments, the population comprises 5×10^6 said stem cells. In certain embodiments, the population comprises 1×10^7 said stem cells. In certain embodiments, the population comprises 5×10^7 said stem cells. In certain embodiments, the population comprises 1×10^8 said stem cells. In certain embodiments, the population comprises 5×10^8 said stem cells. In certain embodiments, the population comprises 1×10^9 said stem cells. In certain embodiments, the population comprises 5×10^9 said stem cells. In certain embodiments, the population comprises 1×10^{10} said stem cells. In certain embodiments, the stem cells have been passaged at least, about, or no more than 5 times. In certain embodiments, the stem cells have been passaged at least, about, or no more than 10 times. In certain embodiments, the stem cells have been passaged at least, about, or no more than 15 times. In certain embodiments, the stem cells have been passaged at least, about, or no more than 20 times. In certain embodiments, the population has been expanded.

[0048] In certain embodiments, the implantable scaffolding substrate is selected from the group consisting of a β-tricalcium phosphate substrate, a β-tricalcium phosphate-collagen

substrate, a collagen substrate, a calcium phosphate substrate, a mineralized human placental collagen substrate, a hyaluronic acid substrate, and a ceramic substrate. In certain embodiments, the implantable scaffolding substrate is a β-tricalcium phosphate substrate. In certain embodiments, the implantable scaffolding substrate is a β-tricalcium phosphate-collagen substrate. In certain embodiments, the implantable scaffolding substrate is a collagen substrate. In certain embodiments, the implantable scaffolding substrate is a calcium phosphate substrate. In certain embodiments, the implantable scaffolding substrate is a mineralized human placental collagen substrate.

[0049] In another aspect, provided herein is a method for formulating an injectable composition, comprising combining a population of placental stem cells with injectable hyaluronic acid or collagen. In certain embodiments, the stem cells are nonadherent. In certain embodiments, the stem cells are $CD34^+$. In certain embodiments, the stem cells are $CD44^-$. In certain embodiments, the said stem cells are $CD34^+$ and $CD44^-$. In certain embodiments, the said stem cells are $CD9^+$, $CD54^+$, $CD90^+$, or $CD166^+$. In certain embodiments, the said stem cells are $CD9^+$, $CD54^+$, $CD90^+$, and $CD166^+$. In certain embodiments, the said stem cells are $CD31^+$, $CD117^+$, $CD133^+$, or $CD200^+$. In certain embodiments, the said stem cells are $CD31^+$, $CD117^+$, $CD133^+$, and $CD200^+$. In certain embodiments, at least about 70% of said cells are $CD34^+$ and $CD44^-$ stem cells. In certain embodiments, the at least about 90% of said cells are $CD34^+$ and $CD44^-$ stem cells. In certain other embodiments, the placental stem cells are adherent. In specific embodiments, the placental stem cells are $CD200^+$ and HLA-G^+; $CD73^+$, $CD105^+$, and $CD200^+$; $CD200^+$ and OCT-4^+; $CD73^+$, $CD105^+$ and HLA-G^+; $CD73^+$ and $CD105^+$ and facilitates the formation of one or more embryoid-like bodies in a population of placental cells comprising said stem cell when said population is cultured under conditions that allow the formation of an embryoid-like body; or OCT-4^+ and facilitates the formation of one or more embryoid-like bodies in a population of placental cells comprising the stem cell when said population is cultured under conditions that allow formation of embryoid-like bodies; or any combination thereof. In more specific embodiments of the nonadherent placental stem cells, the isolated $CD200^+$, HLA-G^+ stem cell is $CD34^-$, $CD38^-$, $CD45^-$, $CD73^+$ and $CD105^+$; the isolated $CD73^+$, $CD105^+$, and $CD200^+$ stem cell is $CD34^-$, $CD38^-$, $CD45^-$, and HLA-G^+; the isolated $CD200^+$, OCT-4^+ stem cell is $CD34^-$, $CD38^-$, $CD45^-$, $CD73^+$, $CD105^+$ and HLA-G^+; the isolated stem cell of claim 1, wherein said $CD73^+$, $CD105^+$ and HLA-G^+ stem cell is $CD34^-$, $CD45^-$, OCT-4^+ and $CD200^+$; the isolated $CD73^+$ and $CD105^+$ stem cell that facilitates the formation of one or more embryoid-like bodies is $OCT4^+$, $CD34^-$, $CD38^-$ and $CD45^-$; and/or the isolated OCT-

4^+ and which facilitates the formation of one or more embryoid-like bodies is $CD73^+$, $CD105^+$, $CD200^+$, $CD34^-$, $CD38^-$, and $CD45^-$. In certain embodiments, the population of placental stem cells has been expanded. In certain embodiments, the said composition comprises injectable hyaluronic acid. In certain embodiments, the composition comprises injectable collagen. Provided herein are also compositions comprising a population of nonadherent stem cells and injectable hyaluronic acid or collagen.

[0050] In another aspect, provided herein is a method for treating bone defects in a subject, comprising administering to a subject in need thereof an implantable or injectable composition comprising a population of stem cells provided herein, thereby treating the bone defect in the subject. In certain embodiments, the bone defect is an osteolytic lesion associated with a cancer, a bone fracture, or a spine, *e.g.*, in need of fusion. In certain embodiments, the osteolytic lesion is associated with multiple myeloma, bone cancer, or metastatic cancer. In certain embodiments, the bone fracture is a non-union fracture. In certain embodiments, an implantable composition comprising a population of nonadherent stem cells is administered to the subject. In certain embodiments, an implantable composition is surgically implanted, *e.g.*, at the site of the bone defect. In certain embodiments, an injectable composition comprising a population of nonadherent stem cells is administered to the subject. In certain embodiments, an injectable composition is surgically administered to the region of the bone defect. In certain embodiments, the injectable composition is systemically administered.

[0051] In certain embodiments, the stem cells are nonadherent. In certain embodiments, the stem cells are $CD34^+$. In certain embodiments, the stem cells are $CD44^-$. In certain embodiments, the stem cells are $CD34^+$ and $CD44^-$. In certain embodiments, the stem cells are $CD9^+$, $CD54^+$, $CD90^+$, or $CD166^+$. In certain embodiments, the stem cells are $CD9^+$, $CD54^+$, $CD90^+$, and $CD166^+$. In certain embodiments, the stem cells are $CD31^+$, $CD117^+$, $CD133^+$, or $CD200^+$. In certain embodiments, the stem cells are $CD31^+$, $CD117^+$, $CD133^+$, and $CD200^+$. In certain embodiments, at least about 70% of the cells are $CD34^+$ and $CD44^-$ stem cells. In certain embodiments, at least about 90% of the cells are $CD34^+$ and $CD44^-$ stem cells. In certain other embodiments, the placental stem cells are adherent. In specific embodiments, the placental stem cells are $CD200^+$ and HLA-G^+; $CD73^+$, $CD105^+$, and $CD200^+$; $CD200^+$ and OCT-4^+; $CD73^+$, $CD105^+$ and HLA-G^+; $CD73^+$ and $CD105^+$ and facilitates the formation of one or more embryoid-like bodies in a population of placental cells comprising said stem cell when said population is cultured under conditions that allow the formation of an embryoid-like body; or OCT-4^+ and facilitates the formation of one or

more embryoid-like bodies in a population of placental cells comprising the stem cell when said population is cultured under conditions that allow formation of embryoid-like bodies; or any combination thereof. In more specific embodiments of the nonadherent placental stem cells, the isolated $CD200^+$, $HLA\text{-}G^+$ stem cell is $CD34^-$, $CD38^-$, $CD45^-$, $CD73^+$ and $CD105^+$; the isolated $CD73^+$, $CD105^+$, and $CD200^+$ stem cell is $CD34^-$, $CD38^-$, $CD45^-$, and $HLA\text{-}G^+$; the isolated $CD200^+$, $OCT\text{-}4^+$ stem cell is $CD34^-$, $CD38^-$, $CD45^-$, $CD73^+$, $CD105^+$ and $HLA\text{-}G^+$; the isolated stem cell of claim 1, wherein said $CD73^+$, $CD105^+$ and $HLA\text{-}G^+$ stem cell is $CD34^-$, $CD45^-$, $OCT\text{-}4^+$ and $CD200^+$; the isolated $CD73^+$ and $CD105^+$ stem cell that facilitates the formation of one or more embryoid-like bodies is $OCT4^+$, $CD34^-$, $CD38^-$ and $CD45^-$; and/or the isolated $OCT\text{-}4^+$ and which facilitates the formation of one or more embryoid-like bodies is $CD73^+$, $CD105^+$, $CD200^+$, $CD34^-$, $CD38^-$, and $CD45^-$. In certain embodiments, the population has been expanded.

[0052] In yet another aspect, provided herein is a method of producing a cell population comprising selecting cells that a) adhere to a substrate, and b) express CD34 and do not express CD44, and isolating said cells from other cells to form a cell population. In certain embodiments, the method further comprises isolating said cells from other cells to form a cell population. In certain embodiments, the method of producing a cell population, comprises selecting cells that (a) adhere to a substrate, (b) express CD34 and do not express CD44, and (c) facilitate the formation of mineralized matrix in a population of placental cells when said population is cultured under conditions that allow for the formation of a mineralized matrix; and isolating said cells from other cells to form a cell population. In certain embodiments, the said substrate comprises fibronectin. In certain embodiments, provided herein is a method of producing a cell population comprising selecting cells that a) do not adhere to a substrate, and b) express CD34 and do not express CD44, and isolating said cells from other cells to form a cell population. In certain embodiments, the method further comprises isolating said cells from other cells to form a cell population. In certain embodiments, the method of producing a cell population, comprises selecting cells that (a) do not adhere to a substrate, (b) express CD34 and do not express CD44, and (c) facilitate the formation of mineralized matrix in a population of placental cells when said population is cultured under conditions that allow for the formation of a mineralized matrix; and isolating said cells from other cells to form a cell population. In certain embodiments, the said substrate comprises fibronectin. In certain embodiments, the method comprises selecting cells that express at least one of the following: CD9, CD29, CD54, CD90, CD166, or a combination of the foregoing. In certain embodiments, the method comprises selecting cells that express at least

one of the following: CD31, CD34, CD117, CD133, CD200, or a combination of the foregoing.

[0053] In certain embodiments, the selecting is accomplished using an antibody. In certain embodiments, the selecting is accomplished using flow cytometry. In certain embodiments, the selecting is accomplished using magnetic beads. In certain embodiments, the selecting is accomplished by fluorescence-activated cell sorting. In certain embodiments, the cell population is expanded.

[0054] In certain embodiments, the stem cells are $CD34^+$ and $CD44^-$, wherein the cells have been cryopreserved, and wherein the population is contained within a container. In certain embodiments, the cells have been cryopreserved, and wherein said population is contained within a container, and wherein said stem cells form a mineralized matrix when cultured under conditions allowing the formation of a mineralized matrix.

[0055] In certain embodiments, the container is a bag suitable for the intravenous delivery of a liquid. In certain embodiments, the population comprises 1×10^6 said stem cells. In certain embodiments, the population comprises 5×10^6 said stem cells. In certain embodiments, the population comprises 1×10^7 said stem cells. In certain embodiments, the population comprises 5×10^7 said stem cells. In certain embodiments, the population comprises 1×10^8 said stem cells. In certain embodiments, the population comprises 5×10^8 said stem cells. In certain embodiments, the population comprises 1×10^9 said stem cells. In certain embodiments, the comprises 5×10^9 said stem cells. In certain embodiments, the population comprises 1×10^{10} said stem cells. In certain embodiments, the stem cells have been passaged no more than 5 times. In certain embodiments, the stem cells have been passaged no more than 10 times. In certain embodiments, the stem cells have been passaged no more than 15 times. In certain embodiments, the stem cells have been passaged no more than 20 times. In certain embodiments, the stem cells have been expanded within said container. In certain embodiments, the said population is contained in a 0.9% NaCl solution.

[0056] In another aspect, provided herein is a method of producing osteogenic cells comprising culturing a plurality of placental stem cells or a population of isolated placental stem cells, under conditions in which said stem cells differentiate into osteogenic cells, said culturing being for a time sufficient for said osteogenic cells to produce, or facilitate the production of, detectable amounts of mineralized calcium.

[0057] In another aspect, provided herein is a method for formulating an matrix, comprising combining a population of placental stem cells with an implantable scaffolding substrate, wherein said stem cells are $CD34^+$ and $CD44^-$. In certain embodiments, the stem cells are